

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

5 a) a nucleotide sequence encoding an isolated mammalian Bcl-xL binding domain, wherein said isolated mammalian Bcl-xL binding domain has 70% amino acid sequence identity with a Bcl-xL binding domain set forth in SEQ ID NO:2.

10 b) a nucleotide sequence encoding an isolated mammalian Bcl-xL binding domain, wherein said nucleotide sequence hybridizes to the complement a nucleotide sequence set forth in SEQ ID NO:1 which encodes a Bcl-xL binding domain in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C

c) a nucleotide sequence encoding an isolated mammalian Bcl-xL binding domain as shown in SEQ. ID NO:1.

15 2. The isolated nucleic acid molecule of claim 1 wherein the isolated Bcl-xL binding domain consists of amino acids 419-559 or amino acids 429-559 of SEQ. ID NO:2.

3. The isolated nucleic acid molecule of claim 1, wherein said isolated mammalian Bcl-xL binding domain modulates apoptosis in a neural cell.

20 4. The isolated nucleic acid molecule of claim 1, wherein said nucleic acid molecule encodes a fusion protein.

6. An isolated polypeptide selected from the group consisting of:

25 a) a polypeptide comprising an isolated mammalian Bcl-xL binding domain, wherein said isolated Bcl-xL binding domain consists of an amino acid sequence having at least 70% identity with a Pablo Bcl-xL binding domain shown in SEQ. ID NO:2.

b) a polypeptide comprising a Bcl-xL binding domain, wherein said Bcl-xL binding domain consists of an amino acid sequence having at least 70% identity with a Pablo Bcl-xL

binding domain shown in SEQ ID NO:2, provided said polypeptide is not a full-length Pablo polypeptide

c) polypeptide comprising a Bcl-xL binding domain shown in SEQ. ID NO:2.

5 7. A polypeptide comprising an isolated Bcl-xL binding domain set forth in SEQ ID NO:2.

8. The polypeptide of claim 7, within which a conservative amino acid substitution has been made.

10 9. A polypeptide consisting of an isolated Bcl-xL binding domain set forth in SEQ ID NO:2.

15 10. The polypeptide of claim 6, wherein said isolated Bcl-xL binding domain consists of amino acids 419-559 or amino acids 429-559.

11. The polypeptide of claim 6, wherein said isolated Bcl-xL binding domain modulates apoptosis in a neural cell.

20 12. A fusion protein comprising a first polypeptide consisting of an isolated Bcl-xL binding domain and a second, non-Pablo polypeptide.

25 13. An isolated nucleic acid molecule which is antisense to the portion of SEQ ID NO:1 which encodes a Bcl-xL binding domain.

14. A vector comprising the nucleic acid molecule of claim 1.

30 15. A neural cell line stably expressing a heterologous Pablo polypeptide or an isolated Bcl-xL binding domain set forth in SEQ ID NO:2.

16. A nonhuman transgenic animal which contains cells carrying a nucleic acid molecule encoding an isolated mammalian Bcl-xL binding domain.

17. A method of modulating apoptosis in a cell comprising modulating the activity of a Pablo polypeptide or Bcl-xL binding domain thereof.

18. A method of modulating apoptosis in a cell comprising modulating the expression of a Pablo polypeptide or Bcl-xL binding domain thereof.

19. A method for treating a nervous system disorder in a subject comprising modulating the expression or activity of Pablo in a cell of the subject to thereby treat a nervous system disorder in the subject.

20. A method for identifying a compound that modulates the pro-apoptotic activity of a Bcl-xL binding domain, comprising:
contacting a cell expressing a Bcl-xL binding domain with a test compound and;
determining the ability of the test compound to modulate the activity of a Bcl-xL binding domain to thereby identify a compound that modulates the pro-apoptotic activity of a Bcl-xL binding domain.

21. A method for identifying a compound that modulates the pro-apoptotic activity of a Bcl-xL binding domain, comprising:
contacting a cell-free mixture comprising a Bcl-xL binding domain with a test compound and;
determining the ability of the test compound to modulate the activity of a Bcl-xL binding domain to thereby identify a compound that modulates the pro-apoptotic activity of a Bcl-xL binding domain.

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B1

ADD
C1

ADD
D3